

CLAIMS

1. An agent for treating cartilage-related disease comprising as an active ingredient a substance having an EP2 and/or EP3 agonist activity.
2. The agent for treating cartilage-related disease according to claim 1, which is an agent for treating cartilage disorder.
3. The agent for treating cartilage-related disease according to claim 1, which is an agent for producing a cartilage graft.
4. The agent for treating cartilage-related disease according to claim 2 or 3, which has one or more effects selected from stimulating chondrogenesis, stimulating chondrocyte growth, stimulating chondrocyte differentiation, inhibiting cartilage calcification and inhibiting cartilage degradation.
5. The agent for treating cartilage-related disease according to claim 3, which is an agent for chondrocyte culture.
6. The agent for treating cartilage-related disease according to claim 2 or 3, which has one or more effects selected from stimulating integrin mRNA expression, stimulating fibronectin mRNA expression, stimulating cyclin D1 mRNA expression and inhibiting osteopontin mRNA expression.
7. The agent for treating cartilage-related disease according to claim 4, wherein the one or more effects selected from stimulating chondrogenesis, stimulating chondrocyte growth, stimulating chondrocyte differentiation, inhibiting cartilage calcification and inhibiting cartilage degradation is/are based on one or more effects selected from stimulating integrin mRNA expression, stimulating fibronectin mRNA expression, stimulating cyclin D1 mRNA expression and inhibiting osteopontin mRNA expression on a chondrocyte or a cartilage tissue.

8. The agent for treating cartilage-related disease according to claim 7, wherein the effect of stimulating chondrocyte growth is based on stimulating cyclin D1 mRNA expression.
9. The agent for treating cartilage-related disease according to claim 7, wherein the effect of inhibiting cartilage calcification is based on inhibiting osteopontin mRNA expression.
10. An agent for treating cartilage-related disease comprising a combination of one or more substances selected from transforming growth factor- β , insulin-like growth factor, basic fibroblast growth factor, epidermal growth factor, growth hormone and platelet-derived growth factor, and the substance having an EP2 and/or EP3 agonist activity according to claim 1.
11. A method for treating cartilage-related disease, which comprises administering a substance having an EP2 and/or EP3 agonist activity.
12. A method for producing a cartilage graft, which comprises adding a substance having an EP2 and/or EP3 agonist activity.
13. Use of a substance having an EP2 and/or EP3 agonist activity, for the preparation of an agent for treating cartilage disorder or for the preparation of an agent for producing a cartilage graft.
14. The agent for treating cartilage-related disease according to claim 1, wherein the substance having an EP2 agonist activity is one or more compounds selected from a compound described in EP860430, a compound described in WO99/33794, a compound described in EP974580, a compound described in WO2003/74483, a compound described in WO95/19964, a compound described in WO98/28264, a compound described in WO99/19300,

a compound described in EP0911321, a compound described in US4,132,738 and a compound described in US3,965,143.

15. The agent for treating cartilage-related disease according to claim 14, wherein the compound is one or more compounds selected from

- (1) (5Z,9 β ,11 α ,13E)-17,17-propano-11,16-dihydroxy-9-chloro-20-norprosta-5,13-dienoic acid,
- (2) (5Z,9 β ,11 α ,13E)-17,17-propano-11,16-dihydroxy-9-chloroprosta-5,13,19-trienoic acid,
- (3) trans-2-(4-(1-hydroxyhexyl)phenyl)-5-oxocyclopentaneheptanoic acid,
- (4) 2-[3-(4-tert-butylbenzyl)-N-(pyridin-3-ylsulfonyl)amino-methyl]phenoxy]acetic acid,
- (5) [1R[1 α ,2 β (1E,4R*),3 α]]-3-hydroxy-2-[4-hydroxy-4-(1-propylcyclobutyl)-1-butenyl]-5-oxocyclopentane-heptanoic acid methyl ester,
- (6) (2R,3R,4R)-4-hydroxy-2-(7-hydroxyheptyl)-3-[(E)-(4RS)-(4-hydroxy-4-methyl-1-octenyl)]cyclopentanone, and
- (7) (+/-)-15-deoxy-16- α , β -hydroxy-16-methyl PGE1 methylester.

16. The agent for treating cartilage-related disease according to claim 1, wherein the substance having an EP3 agonist activity is one or more compounds selected from a compound described in WO98/34916, a compound described in JP-A-8-239356, a compound described in US4,692,464, a compound described in JP-A-61-249951, a compound described in US4,863,961 and a compound described in US3,985,791.

17. The agent for treating cartilage-related disease according to claim 16, wherein the compound is one or more compounds selected from

- (1) 11 α ,15 α -dimethoxy-9-oxoprosta-5Z,13E-dienoic acid,
- (2) 2-[5-[2-[N-(diphenylmethyl)carbamoyl]ethyl]naphthalen-1-yloxy]acetic acid,
- (3) (1S,5S,6R,7R)-5-[7-hydroxy-6-[3(S)-hydroxy-3-methyl-1(E)-octenyl]bicyclo[3.3.0]oct-2-ene-3-yl]pentanoic acid,

- (4) (-)-[1(R)-[1 α (Z),2 β (R*),3 α]]-7-[3-hydroxy-2-(2-hydroxy-3-phenxypropoxy)-5-oxocyclopentyl]-4-heptenoic acid 4-(benzoylamino)phenylester,
- (5) methyl-7-(2 β -(6-(1-cyclopentyl-yl)-4R-hydroxy-4-methyl-1E,5E-hexadienyl)-3 α -hydroxy-5-oxo-1R,1 α -cyclopentyl)-4Z-heptenoic acid, and
- (6) 9-oxo-11 α ,15 α -dihydroxy-16-phenoxy-17,18,19,20-tetranorprosta-4,5,13-trans-trienoic acid methyl ester.

18. The agent for treating cartilage-related disease according to claim 1, wherein the compound having an EP3 agonist activity is 16-phenoxy- ω -17,18,19,20-tetranor-PGE₂ methylsulfonamide or a salt thereof.

19. A method for screening the agent for treating cartilage-related disease according to claim 1.